1998

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SURVEILLANCE FOR SIN NOMBRE VIRUS AND HANTAVIRUS PULMONARY SYNDROME IN CALIFORNIA, 1993 TO 1997

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ABSTRACT: Hantavirus Pulmonary Syndrome (HPS), a severe and frequently fatal respiratory disease, was first recognized in 1993 during an outbreak of acute illness in the Four Corners area of the southwestern United States. The etiologic agent, Sin Nombre virus (SNV), was identified as a previously unrecognized member of the Hantavirus genus transmitted by rodents, especially members of the genus *Peromyscus*, which shed SNV in urine and feces. Since 1993, 16 California residents have been diagnosed with HPS, four of these were identified retrospectively with onset prior to 1993. The median age of case-patients was 42 years, 10 were male, and eight died. Sites of likely exposure for these cases tended to cluster in the eastern Sierra Nevada range. Serologic surveillance of rodents has been conducted prospectively in California since 1993 and retrospectively for specimens collected back to 1975. To date, serologic evidence of infection with SNV has been recognized in 473 (6.6%) of 7,191 rodents from 18 genera, and in 426 (9.6%) of 4,489 *Peromyscus* spp. At least one seroreactive *Peromyscus* sp. specimen has been identified in 40 of 46 counties surveyed.

KEY WORDS: hantavirus, hantavirus pulmonary syndrome, Sin Nombre virus, deermice, *Peromyscus*

Proc. 18th Vertebr. Pest Conf. (R.O. Baker & A.C. Crabb, Eds.) Published at Univ. of Calif., Davis. 1998.

INTRODUCTION

Hantavirus pulmonary syndrome (HPS) was first recognized in 1993 when an outbreak of an acute illness of unknown etiology occurred among residents of the Four Corners area in the southwestern United States (CDC 1994). The illness was characterized by a prodrome of fever and flu-like symptoms which rapidly progressed to respiratory distress and was frequently fatal. The etiologic agent was identified as a previously unrecognized member of the Hantavirus genus that was given the provisional name of Sin Nombre virus (SNV). Rodents, especially members of the genus *Peromyscus*, were identified as the principal reservoir of the virus, which they shed in urine and feces.

Since 1993, the California Department of Health Services, in cooperation with local health agencies and vector control programs, has conducted surveillance for hantavirus in human and non-human mammals in California. This report summarizes results of this surveillance from 1993 to 1997.

METHODS

HPS Cases

Passive surveillance for HPS cases is conducted through the Division of Communicable Disease Control of the California Department of Health Services (DHS). Serologic testing of suspect HPS patients is provided through the Viral and Rickettsial Diseases Laboratory (VRDL), DHS. A suspect HPS case is defined as a previously healthy patient experiencing a febrile illness (i.e., temperature greater than 101° F) characterized by bilateral diffuse interstitial edema that may radiographically resemble adult respiratory distresss syndrome, with respiratory compromise requiring supplemental oxygen, developing within 72 hours of hospitalization (CDC 1998). California health care providers desiring serologic testing of a suspect HPS case are requested to submit 5 to 10 ml of acute whole blood to the VRDL. An immunofluorescent antibody procedure with SNV antigen is used for testing for hantavirus antibody activity in serum specimens. An attempt is made to obtain a convalescent blood sample on all patients for whom the acute specimen was reactive. For fatal cases, specimens of lung and kidney tissue are requested.

Information on the suspect patient's acute illness is collected in the case history form which accompanies the serologic specimen and, in the event of a confirmed case, through detailed abstraction of the complete medical record. Information on the patient's work-related and recreational activities, place of residence, and recent travel are collected from the patient or a proxy to assist in determining the likely circumstances of exposure. On-site investigations of the patient's residence and other likely exposure locales are conducted by public health biologists and environmental health specialists from the state and local health departments.

Rodent Surveillance

As part of the environmental follow-up conducted on all confirmed HPS cases in California, attempts are made to collect blood from rodents at each potential exposure site. Procedures and total trap-nights vary according to the suspected circumstances of the patient's exposure

(e.g., occupational versus peridomestic) and the interval between confirmation of the case and initiation of the environmental follow-up. Blood samples are obtained from collected rodents by intracardiac puncture using a 1 ml. tuberculin hypodermic needle. Blood samples are chilled and shipped on ice to VRDL for processing. Serologic testing is conducted as previously described (Jay et al. 1997). Specimens with antibody activity detectable at a dilution of 1:64 or greater are considered reactive.

In addition to responsive surveillance, since 1993 DHS and other agencies have routinely collected serum specimens for hantavirus evaluation from rodents throughout California. Also, selected archived specimens, including sera, tissues, and whole carcasses, from rodents collected in California back to 1975 have been tested for evidence of hantavirus infection.

RESULTS AND DISCUSSION

HPS cases

Since 1993, 16 California residents have been diagnosed with HPS (Table 1). Four of these were identified retrospectively, with onset of illness having occurred in 1980, 1984, and two in 1992. Eight cases had a fatal outcome. The median age of case-patients was 42 years (range, 22 to 56) and 10 were male. Case-patients were residents of 11 counties—Alameda, Contra Costa, Inyo (2), Kern, Modoc, Mono (4), Nevada (2), Plumas, Santa Barbara, San Bernardino, and San Francisco (Figure 1). Probable sites of exposure included the counties of Inyo (2), Modoc, Mono (4 or 5), Nevada (2), Placer, Plumas, and Santa Barbara, and the states of New Mexico (2) and Washington. Probable exposure site could not be reliably determined for one case. The circumstances of exposure were peridomestic for seven cases, occupational for four, recreational for three, and unknown for two. Detailed clinical and epidemiologic features of select California HPS cases have been previously described (Flood et al. 1995; Schwarcz et al. 1996; Shefer et al. 1994; Jay et al. 1996).

Rodent Surveillance

Testing for hantavirus seroreactivity in California mammals has been performed on specimens from 7,295 animals, representing 51 species of 27 genera. Among the 18 genera of rodents evaluated, evidence of hantavirus seroreactivity has been identified in seven (Table 2). Six species of the genus *Peromyscus* have demonstrated the most consistent seroreactivity; 426 (9.6%) of 4,489 *Peromyscus* spp. tested had detectable antibody to SNV (Table 3). At least one seroreactive *Peromyscus* specimen has been identified in 40 of 46 counties sampled (Figure 1).

Reithrodontomys megalotis and *Microtus californicus* specimens have demonstrated evidence of infection with Sin Nombre-like hantaviruses (El Moro Canyon and Isla Vista, respectively), but these strain variations have not been shown to be pathogenic to humans. Seroreactivity has been occasionally identified in *Neotoma* sp., *Perognathus* sp., and *Spermophilus* sp. rodents in California and elsewhere; however, it is believed that these species are incidentally infected with SNV and are not competent reservoirs or vectors. There is no serologic evidence to date of SNV infection in domestic rodent species (i.e., *Mus* spp., *Rattus* spp.), lagomorphs, or wild and domestic carnivores.

ACKNOWLEDGMENTS

Mosquito & Vector Control Districts of California; County Departments of Environmental Health; County Departments of Health Services; California State Polytechnic University, Pomona; University of California, Davis; University of New Mexico; University of Nevada, Reno; California Department of Fish & Game; Special Pathogens Branch, National Center for Infectious Diseases, Centers for Disease Control and Prevention.

LITERATURE CITED

CENTERS FOR DISEASE CONTROL AND PREVENTION. 1993. Hantavirus pulmonary syndrome—United States. MMWR 1994; 43:45-8.

CENTERS FOR DISEASE CONTROL AND PREVENTION. 1997. Case definitions for infectious conditions under public health surveillance. MMWR. 46 (No. RR-10).

FLOOD, J., L. MINTZ, M. JAY, F. TAYLOR, and W. L. DREW. 1995. Hantavirus infection following wilderness camping in Washinton State and northeastern California. West. J. Med. 163:162-4.

JAY, M., M. S. ASCHER, and B. B. CHOMEL, et al. 1997. Seroepidemiologic studies of hantavirus infection among wild rodents in California. Emerg. Infect. Dis. 3:183-90.

JAY, M., B. HJELLE, and R. DAVIS, et al. 1996. Occupational exposure leading to hantavirus pulmonary syndrome in a utility company employee. Clin. Infect. Dis. 22:841-4.

SCHWARCZ, S. K., A. M. SHEFERS, and S. R. ZAKI. 1980. Retrospective diagnosis of a feral case of the hantavirus pulmonary syndrome. West. J. Med. 1996. p. 348-50.

SHEFER, A. M., J. W. TAPPERO, and J. S. BRESEE, et al. 1994. Hantavirus pulmonary syndrome in California: Report of two cases and investigation. Clin. Infect. Dis. 19:1105-9.

Table 1. Hantavirus pulmonary syndrome cases diagnosed in California residents, 1980 to 1997.

Onset	Age	Sex	County of Residence	Outcome	Likely Exposure Location	Exposure Circumstances/ Follow-up Investigation
Feb 1980	22	M	San Francisco	Died	New Mexico	Rodent infestation at adobe home in NM
Feb 1984	34	F	Inyo	Died	Deep Springs, Inyo Co.	Heavy rodent infestation at residence
Sep 1992	29	M	Santa Barbara	Died	Solvang, Santa Barbara Co.	Trapped and handled rodents prior to illness
Aug 1992	49	F	Alameda	Died	Mono Co. or WA State	Backpacked in Mono Co. and WA 2 to 4 weeks prior to illness
Jul 1993	27	F	Mono	Died	Mammoth Lakes, Mono Co.	Two strains of SNV isolated from rodents near patient's worksite
Mar 1994	42	F	San Bernardino	Survived	New Mexico	SNV(+) rodents from NM residence; no SNV(+) rodents from CA residence
May 1994	42	M	Kern	Died	Undetermined	Cleaned out rodent-infested building prior to onset; no SNV(+) rodents at residence or worksite
Sep 1994	56	M	Mono	Survived	Lee Vining, Mono Co.	SNV(+) rodents at patient's residence and worksite (7 of 42)
Feb 1995	42	F	Mono	Survived	Walker, Mono Co.	Swept out garage with rodent droppings; SNV(+) rodents at patient's residence (3 of 22)
Mar 1995	47	M	Nevada	Survived	Nevada Co.	SNV(+) rodents at patient's residence (11 of 13) and worksite (6 of 19)
Jun 1995	45	M	Mono	Died	Crowley Lake, Mono Co.	Cleaned rodent-infested home; SNV(+) rodents at residence (6 of 11)
Aug 1995	55	M	Contra Costa	Died	Cisco Grove, Placer Co.	Camped in Sierra Nevada; SNV isolated from Placer Co. rodent matched patient isolate
Sep 1995	32	F	Plumas	Survived	Graeagle, Plumas Co.	SNV isolated from 1 of 21 Plumas Co. rodents matched patient isolate
Jul 1996	49	M	Modoc	Survived	Alturas, Modoc Co.	SNV(+) rodents at residence (1 of 3) and other nearby sites (9 of 62)
Jul 1997	43	M	Nevada	Survived	Tahoe-Donner, Nevada Co.	Hiked in Tahoe-Donner; SNV(+) rodents at hiking trails (5 of 16) and areas near home (22 of 71)
Oct 1997	38	M	Inyo	Survived	Bishop, Inyo Co.	Noted rodent excreta at worksites; SNV(+) rodents at worksite (2 of 23)

Table 2. Serologic results of surveillance for hantavirus in rodents collected in California, 1975 to 1997.

Species	Number Collected	Number Reactive (%)
Ammospermophilus leucurus	4	0
Chaetodipus californicus	17	0
Clethrionomys spp.	1	0
Dipodomys spp.	40	1 (2.5%)
Glaucomys sabrinus	1	0
Microtus spp.[1]	41	7 (17.1%)
Mus musculus	119	0
Neotoma spp.	534	6 (1.1%)
Onychomys torridus	1	0
Perognathus spp.	72	2 (2.8%)
Peromyscus boylii	196	3 (1.5%)
P. californicus	328	10 (3.0%)
P. crinitus	44	3 (6.8%)
P. eremicus	179	4 (2.2%)
P. maniculatus	3,349	390 (11.6%)
P. truei	348	15 (4.3%)
Peromyscus sp.	45	1 (2.2%)
Rattus spp.	146	0
Reithrodontomys megalotis[2]	205	30 (14.6%)
Sciurus griseus	1	0
Sigmodon hispidus	14	0
Spermophilus spp.	1,228	1 (0.1%)
Tamias spp.	270	0
Tamiasciurus douglasii	8	0

[1]Isla Vista virus

[2]El Moro Canyon virus

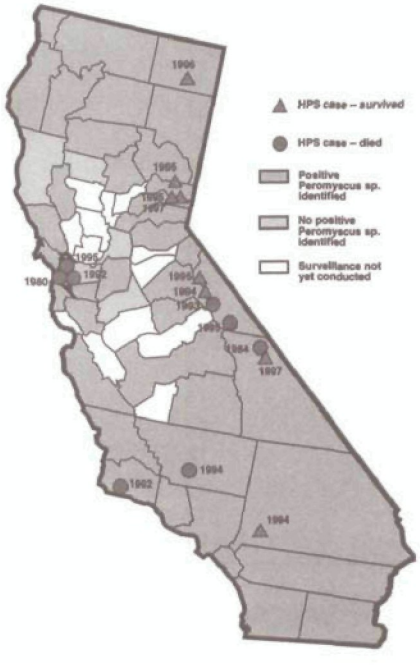

Figure 1. Distribution of hantavirus pulmonary syndrome (HPS) human cases (by county of residence) and *Peromyscus* spp. seroreactive to Sin Nombre virus in California, 1975 to 1997.

Table 3. Serologic results of surveillance for Sin Nombre virus among *Peromyscus* spp. in California, 1975 to 1997.

County[1]	Number Collected	Number Reactive (%)
Alameda	6	1 (16.7%)
Alpine	55	11 (20.0%)
Butte	145	15 (10.3%)
Contra Costa	36	0
Del Norte	54	1 (1.9%)
El Dorado	51	6 (11.8%)
Fresno	249	34 (13.7%)
Glenn	8	0
Humboldt	61	5 (8.2%)
Imperial	18	3 (16.7%)
Inyo	37	3 (8.1%)
Kern	84	7 (8.3%)
Lake	49	4 (8.2%)
Lassen	32	3 (9.4%)
Los Angeles	326	15 (4.6%)
Marin	92	3 (3.3%)
Mendocino	19	0
Merced	78	8 (10.3%)
Modoc	77	11 (14.3%)
Mono	176	34 (19.3%)
Monterey	130	6 (4.6%)
Mariposa	58	7 (12.1%)
Nevada	139	52 (37.4%)
Orange	268	10 (3.7%)
Placer	29	2 (6.9%)
Plumas	67	14 (20.9%)
Riverside	217	2 (0.9%)
Sacramento	36	0
San Bernardino	89	3 (3.4%)
San Diego	447	15 (3.4%)
San Francisco	30	0
San Mateo	81	2 (2.5%)
Santa Barbara	352	89 (25.3%)
Santa Clara	103	1 (1.0%)
Shasta	37	4 (10.8%)
Sierra	48	9 (18.8%)
Siskiyou	122	13 (10.7%)
San Joaquin	11	1 (9.1%)
San Luis Obispo	94	6 (6.4%)
Sonoma	143	3 (2.1%)
Stanislaus	15	0
Tehama	35	5 (14.3%)
Trinity	24	8 (33.3%)
Tulare	20	2 (10.0%)
Tuolumne	32	1 (3.1%)
Ventura	237	11 (4.6%)
Total	4,517	430 (9.5%)

[1]Counties in which surveillance for hantavirus in rodents has yet to be conducted are not listed.